Gastroenterology and Hepatology From Bed to Bench.

EDITORIAL

Emergence of resistant *salmonella* spp.; new challenges, new trends

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Salmonella enterica is a common cause of human food borne gastroenteritis and bacteremia worldwide. Salmonellosis is caused by different serotypes of *salmonella*; humans and animals are generally infected with these bacteria by the consumption of contaminated food products (1-3). Non-typhi *salmonella* gastroenteritis in contrast to the invasive salmonellosis that requires prompt antibiotic therapy, is usually self-limited (4). According to the WHO license for the treatment of salmonellosis in last decades, increasing usage of antimicrobial agents in clinics and slaughterhouses is becoming a major problem (5).

Chloramphenicol, sulfamethoxazole-trimethoprim, and ampicillin were the earliest antibiotics used the treatment of salmonellosis.

However, following the development of resistance to the aforementioned drugs, quinolones and cephalosporines are currently in use (6). The usage of quinolones and cephalosporines in the veterinary world as the therapeutic agents or growth factors led to the emergence of highly resistant veterinary *Salmonella* strains which might transfer into human via the food chain process. This transmission will cause failure in clinical treatment of related diseases (7, 8).

Frequency of antimicrobial resistance found among isolates from human is directly linked to their use in animals (9). Evaluation of the results of regional studies especially in the countries with uncontrolled use of antibiotics has revealed a significant increase in the number of resistant strains, principally in animal foods as growth factors or therapeutic agents (10-12).

Resistance to the aforementioned antibiotics is either chromosomal or plasmid-encoded. Different molecular mechanisms are responsible for the occurrence of resistance against antibiotics in *Salmonella spp.* (13). Transmissibility of the plasmid-encoded resistant phenotypes among enteric bacteria within the gastrointestinal tract and environment has resulted to a change in the use of the first-line antibiotics against salmonellosis towards antibiotics with no identified similar resistant mechanisms, i.e., quinolones, as the last choice in treatment strategy. New studies in this context have demonstrated the emergence of great numbers of quinolone resistant serotypes in recent years (6, 14, 15).

Studies about the aforementioned bacteria have revealed new mechanism of resistance for this group of antibiotics. Mutation in DNA gyrase A/B, topoisomerase IV and plasmid-mediated resistance due to (Qnr), Aac (6′)-Ib-cr, and QepA efflux genes in both of human and animal isolates are three major types of resistance mechanisms in these bacteria. Transmission of these plasmids from other enteric bacteria and natural selection of chromosomally mutated strains could be

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responsible for the emergence of this type of resistance (16).

On the basis of our findings, regarding the regional screening study of the resistance patterns among different *S. enterica* serotypes isolated from humans, the highest rates of antibiotic resistance were as follows: nalidixic acid; 45.7%, trimethoprim-sulfamethoxazole; 36.4%, ampicillin 15.5%, chloramphenicol; 14.7%, and cephalothin; 6.2% (11). Similar result was found in another study in Iran (12). Most of these isolates have carried mutations on gyrA gene (14). In a new study in USA, the plasmid harboring quinolon resistant bacteria was identified in all of the plasmid harboring human-derived non-typhi enterica isolates of Salmonella spp. (17). According to the report of National Antimicrobial Resistance Monitoring System (NARMS), the increase in MIC ($\geq$ 32 μg/ml) for nalidixic acid in non *typhoidal salmonella* as the last-line antibiotic and increase in their resistance rates from 0.9% to 2% during 1997 – 2008 (for human isolates of *Salmonella enterica* serovar Enteritidis about 1.7% to 6.6%), the need for alternative therapeutic approaches seems necessary (18). It seems foresighted that prescription of new antibiotics in future will not guarantee the successful treatment as a result of present resistance mechanisms in these bacteria.

Eradication of bacteria from their animal sources seems to be the best inhibitory manner for emergence of resistant strains among these bacteria. Nowadays usage of probiotics and prebiotics and competitive exclusion (CE) cultures are considered as successful and acceptable treatments strategies. These methods can help us to control colonization and growth of gastrointestinal pathogens (19).

Exploitation of the mucosal immune system against these bacteria is another useful strategy. Vaccination of animals with an inactived *salmonella* ghost or its related DNA-based vaccines is a suitable method to prevent bacterial colonization in these bacteria. In addition, use of preservative food additives will reduce microbial infections (20, 21). However, the elimination of any possible source of infection for *Salmonella spp.* instead of antibiotic therapy seems to be a well-advised solution for controlling the emergence of more resistant *Salmonella* serotypes.

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